CLAIMS

1. A process for the manufacture of multi-layered tablet dosage of an antihyperglycemic pharmaceutical compositions for once a day administration, the process comprising:

a) preparing a first granule formulations comprising at least one non-biodegradable inert polymer and a biguanide or pharmaceutically acceptable salts thereof of particle size less than 100 microns to achieve pH independent prolonged in-vitro release of biguanide or pharmaceutical acceptable salts thereof;

b) preparing a second granule formulations comprising active pharmaceutical ingredient (API) or APIs or pharmaceutical acceptable salts thereof for immediate release selected from the group of thiazolidinediones, sulfonyl ureas, alpha – glucosidase inhibitor, aldose reductase inhibitor, statins compound, squalene synthesis inhibitor, fibrates, angiotensin converting enzymes inhibitor, LDL catabolism enhancers;

c) treating the first and second granule formulations with lubricants; and

d) compressing the first and second granule formulations to form the multi-layered tablet dosage of the antihyperglycemic pharmaceutical composition, the multi-layered tablet dosage containing layers of the first and second granules formulations.

2. The process of claim 1, wherein the biguanide is Metformin, Buformin, Phenformin or pharmaceutical acceptable salts thereof and thiazolidinedione is Pioglitazone, Rosiglitazone, Troglitazone or pharmaceutically acceptable salts thereof or mixtures thereof.

3. A process as claimed in claim 1, wherein a non-biodegradable inert polymer is selected from the group consisting of cellulose derivatives, (meth)

acrylic acid co-polymers, xanthan gum, guar gum, alginates or pharmaceutical acceptable salt thereof or mixtures thereof.

4. A pharmaceutical composition in multilayer tablet dosage form for once a day administration comprising at least two layers wherein,

i. type I layer comprises at least one non-biodegradable inert polymer and a biguanide or pharmaceutically acceptable salts thereof of particle size less than 100 microns for pH independent prolonged in-vitro release of biguanide or pharmaceutical acceptable salts thereof;

ii. another layer for immediate release of active pharmaceutical ingredient (API) or APIs or pharmaceutical acceptable salts thereof selected from the group of thiazolidinediones, sulfonyl ureas, biguanide, alpha – glucosidase inhibitor, aldose reductase inhibitor, statins compound, squalene synthesis inhibitor, fibrates, angiotensin converting enzymes inhibitor, LDL catabolism enhancers and mixtures thereof.

5. A composition as claimed in claim 4, wherein the biguanide is Metformin, Buformin, Phenformin or pharmaceutical acceptable salts thereof and thiazolidinedione is Pioglitazone, Rosiglitazone, Troglitazone or pharmaceutically acceptable salts thereof or mixtures thereof.

6. A composition as claimed in claim 4, wherein a non-biodegradable inert polymer is selected from the group consisting of cellulose derivatives, (meth)acrylic acid co-polymers, xanthan gum, guar gum, alginates or pharmaceutical acceptable salt thereof or mixtures thereof.

7. A composition as claimed in claim 4, wherein another layer comprising thiazolidinedione is preferably Pioglitazone HCl of particle size less than 30 microns, further comprises at least one excipient selected from fillers, disintegrants and binder.

8. A composition as claimed in claim 6, wherein the cellulose derivatives is selected from alkylcellulose, hydroxyalkylcellulose, carboxyalkylcellulose preferably methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylmethylcellulose, methylhydroxyethylcellulose, hydroxymethylcellulose, hydroxypropylcellulose, carboxymethylcellulose, sodium carboxymethylcellulose and calcium carboxymethylcellulose.

9. A composition as claimed in claim 4, wherein the binary mixture of polymers are selected from the mixture of hydroxypropylmethylcellulose and hydroxypropylcellulose; hydroxypropylmethylcellulose and hydroxyethylcellulose; hydroxypropylmethylcellulose and sodium carboxymethylcellulose; hydroxypropylmethylcellulose and sodium alginate; hydroxypropylmethylcellulose and Xanthan gum ; hydroxypropylmethylcellulose and guar gum; in the ratios ranging from 1 : 0.01 to 1 : 3.5 and are present in an amount of at least 35% by weight of the biguanide, more preferably 40-65 % by weight of the biguanide.

10. A composition as claimed in claim 4, wherein the mixture of three polymers are selected from hydroxypropylmethylcellulose, sodium carboxymethylcellulose and methacrylic acid copolymer; or hydroxypropylmethylcellulose, sodium alginate and methacrylic acid copolymer used in ratios of 1 : 0.01: 0.1 to 1 : 3.5 : 0.5 respectively and are present in an amount of at least 35% by weight of the biguanide, more preferably 40 – 65 % by weight of the biguanide.

11. A composition as claimed in claim 6, wherein the nominal viscosity at 20°C of a 2% w/w aqueous solution of hydroxypropylmethylcellulose used is not less than 3000cP, the nominal viscosity of a 1%w/w aqueous solution of sodium alginate at 20°C is not less than 50cP and the nominal viscosity of a 1%w/w aqueous dispersion of guar gum is not less than 2000 cP.

12. A composition as claimed in claim 6, the nominal viscosity at 25°C of a 1% w/w aqueous solution of hydroxypropylcellulose is not less than 1500cP; hydroxyethylcellulose is not less than 1500cP; sodium carboxymethylcellulose is not less than 1500 cP and xanthan gum is not less than 1200 cP.

13. A composition as claimed in claim 7, wherein disintegrants are selected from the group comprising starch, sodium starch glycollate, crosscarmellose sodium, crospovidone, pregelatinized starch, microcrystalline cellulose and hydroxypropylcellulose.

14. A composition as claimed in claim 4, wherein the pH independent prolonged in-vitro release of biguanide from the type I layer at the end of 1, 4 and 8 hours lies in the range of 25 – 45%w/w, 50 – 80%w/w and not less than 75%w/w respectively and the in-vitro release of API or APIs or pharmaceutical acceptable salts thereof from the immediate release layer at the end of 30 minutes is not less than 80%w/w.

15. A composition as claimed in claim 4, wherein the type I layer comprises Metformin HCl in the range of 500 – 2000mg and another layer comprises Pioglitazone HCl equivalent to Pioglitazone in the range of 15 – 60 mg.

16. A composition as claimed in claim 4, wherein the type I prolonged release layer comprises Metformin HCl in an amount of at least 48%w/w and preferably over 50%w/w of that layer and another immediate release layer comprises Pioglitazone HCl in an amount from 5% to 30% w/w of that layer.

17. A pharmaceutical dosage form of type I granules as claimed in claim 4, exhibiting pH independent prolonged in-vitro release of Metformin HCl, wherein the dosage form comprises at least 48% w/w of Metformin HCl of particle size less than 100 microns and at least one polymer selected from alkylcellulose, hydroxyalkylcellulose and carboxyalkylcellulose or pharmaceutical acceptable

salts thereof, (meth)acrylic acid copolymers, xanthan gum, guar gum, alginates or pharmaceutically acceptable salts thereof, the polymer(s) being present in an amount of at least 35% by weight of Metformin HCl.

18. A process for the preparation of pharmaceutical dosage form of first granules as claimed in claim 1, wherein

iii. Metformin HCl is blended with at least one non-biodegradable inert polymer selected from alkylcellulose, hydroxyalkylcellulose and carboxyalkylcellulose or pharmaceutical acceptable salts thereof, (meth)acrylic acid copolymers, xanthan gum, guar gum, alginates or pharmaceutically acceptable salts thereof to obtain Metformin HCl – polymer blend, the polymer(s) being present in an amount of at least 35% by weight of Metformin HCl and Metformin HCl being present in an amount of at least 48% by weight of dosage form;

iv. the Metformin HCl – polymer blend is wet granulated using water or hydroalcoholic solution optionally containing binder and plasticizer;

v. the granulated mass is dried, sized, lubricated and compressed.

19. A method of treating diabetes in a mammal in need thereof, which comprises administering a pharmaceutical composition in multilayer dosage form comprising at least two layers wherein,

vi. type I layer comprises at least one non-biodegradable inert polymer and a biguanide or pharmaceutically acceptable salts thereof of particle size less than 100 microns for pH independent prolonged in-vitro release of biguanide or pharmaceutical acceptable salts thereof;

vii. another layer for immediate release of active pharmaceutical ingredient (API) or APIs or pharmaceutical acceptable salts thereof selected from the group of thiazolidinediones, sulfonyl ureas, biguanide, alpha – glucosidase inhibitor, aldose reductase inhibitor, statins compound, squalene synthesis inhibitor, fibrates, angiotensin converting enzymes inhibitor, LDL catabolism enhancers and mixtures thereof.

20. A method as claimed in claim 19, wherein the type I layer comprises Metformin HCl and another layer comprises Pioglitazone, Rosiglitazone, Troglitazone or pharmaceutical acceptable salts thereof.